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THESIS

FUNCTIONAL SPECIFICATIONS TO AN AUTOMATED RETINAL SCANNER FOR USE IN PLOTTING THE VASCULAR MAP

by

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December 1988

Thesis Advisor: Gary K. Poock

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The connection between eye disease and diabetes is proven and is no longer a point of conjecture. In focusing attention on the retina, profound inroads have been made in the fight against this dreaded disorder of the blood. By carefully imaging the blood vessels in the back of the eye, medical professionals can make accurate diagnoses based upon the changes and abnormalities observed. In addition, because the vasculature in the retina is extremely sensitive to fluctuations in normal bodily processes, often the first indications of diabetes and many other diseases manifest themselves here and are found during routine eye examinations.

This thesis will explore the possibilities of a new method of retinal imaging by the blending and application of existing technologies. With the use of an automated, infrared-based imaging system, problems related to human error and the limitations of existing methods can be readily resolved and the groundwork can be laid for a new standard of accuracy in retinal imaging. Most importantly, it will automate the entire procedure providing medical specialists heretofore unavailable accuracy in their diagnoses.

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Functional Specifications To An Automated Retinal Scanner For Use In Plotting The Vascular Map

by

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Submitted in partial fulfillment of the requirements for the degree of

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ABSTRACT

The connection between eye disease and diabetes is proven and is no longer a point of conjecture. In focusing attention on the retina, profound inroads have been made in the fight against this dreaded disorder of the blood. By carefully imaging the blood vessels in the back of the eye, medical professionals can make accurate diagnoses based upon the changes and abnormalities observed. In addition, because the vasculature in the retina is extremely sensitive to fluctuations in normal bodily processes, often the first indications of diabetes and many other diseases manifest themselves here and are found during routine eye examinations.

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ACKNOWLEDGEMENT

The author takes great pride in presenting this thesis. However, credit must be attributed where it is justly deserved. Throughout the course of this study many tragic, emotional events have occurred in the author's life and that of his family's which might have caused the cessation of this work on any one of several occasions. It occurred to the author, as this thesis draws to a close, that there has never failed to appear some small occurrence or act that has not provided some bright, hopeful outlook to keep this study progressing ever onward amidst all the emotional turmoil.

It is with this etched permanently in mind that the author would like to acknowledge the courage shown by his father and his wife in their respective battles against cancer. It has been of great personal inspiration to have been witness to their dogged determination in simultaneously overcoming these diseases, from the initial shock of the diagnoses lasting through the daily misery of countless treatments. Despite it all, they always radiated hope and determination, even when the outlook seemed darkest. It is with justifiable pride that he present this study in their honor.

To have been an inconsequential aid in these two herculean struggles has forever instilled in the author an unbounded love for life and an unshakeable belief in the inherent goodness of people. For that reason it is hoped that some good will come from this study; a possible benefit to others so that they may never know the pain of chronic disease.

I. INTRODUCTION

A. BACKGROUND

At the time when diabetes mellitus was first researched, most diabetics died before retinopathy (blood vessel damage and occlusion) severe enough to cause blindness could develop. The discovery of insulin in 1922 prolonged the lives of many of these patients and allowed doctors the opportunity to research the disease's long-term effects, particularly on eyesight. In 1930, diabetes mellitus caused 1% of cases of blindness in the United States; by 1960, this figure had increased to 15%. Today, diabetes is the leading cause of new cases of blindness in this country, afflicting both military active duty and their dependents. Although causes of blindness in diabetic patients include glaucoma, cataract and optic neuropathy, diabetic retinopathy accounts for 84% of cases. An estimated 50,000 patients are legally blind as a result of diabetic retinopathy. [Garcia, 1984, p. 2]

The connection between eye disease and diabetes is proven and, after much careful research, is no longer a point of contention. In focusing attention to the after portion of the eye, the retina, profound inroads have been made in the fight against this dreaded disorder of the blood. By carefully imaging the blood vessels in the back of the eye, medical professionals can make accurate diagnoses based upon the changes and abnormalities observed. In addition, because the blood vessels, or vasculature, in the retina are extremely sensitive to fluctuations in normal bodily processes, often the first indications of diabetes and many other diseases manifest themselves here and are found during routine eye examinations.

Two current procedures are considered the state-of-the-art in retinal imaging: 1) fluorescein angiography and 2) fluorophetometry. Both rely on manual, photographic (visible spectrum) methods to image the retina. Although both procedures provide highly useful information, mapping of the vasculature within the area of the retina remains a painstaking, time-consuming, often painful process for both doctor and patient alike. In addition, individual images of patients' retinas are subject to the inaccuracies of the manual methods used to take those pictures. These include, but are not limited to, inconsistencies in the photographic scale, errors encountered requiring retakes, and diagnostic usefulness of the photographic image over extended periods of time.

This thesis will explore the possibilities of a new method of retinal imaging by the blending and application of existing technologies. With the use of an automated, infrared-based imaging system most of the above problems can be readily resolved and the groundwork for a new standard of accuracy in retinal imaging can be forged. It is felt that with the aid of this proposed system not only will the imaging process be substantially shortened, it will also become a painless procedure for the patient, and, most importantly, automate the entire process providing medical specialists computer accuracy in their diagnoses

It is hoped that this system will vastly improve the diagnostic capability of the medical specialist over both the short and long terms and perhaps lead to further research into the ever-expanding utility provided by the eye in the diagnosis of many bodily afflictions. Both active duty Navy personnel and their dependents will be the direct beneficiaries of such an improvement to the current methods. Despite the obvious importance the Navy puts on the health and medical care of its members, they are no less immune as a group to the vagaries of this disease. If

diabetes does present itself within these members, they will have available an aid in the early detection and continuing treatment of diabetes. Therefore, it is the distinct wish of the author that this system provide some relief to the patients afflicted with diabetes and other vision-impairing ailments, making their lives more full and less burdened with the limitations brought on by their disease.

B. SCOPE

The eye has often been referred to as the "window to the soul" [Griffin, 1977, p.1] and, as such, provides insight to what's going on in the rest of the body. Scientific study of the retina has long concluded that several diseases display their first, telltale signs within this portion of the human anatomy. Most notable among these diseases are diabetes mellitus, and more recently Acquired Immune Deficiency Syndrome (AIDS) [Dosa, 1988, B1].

As diabetes presents an ever-increasing number of blindness cases to the medical professionals concerned with the research and treatment of this disease, the focus of this thesis will be on providing a superior diagnostic tool for use in diagnosis and treatment. While the usefulness of this system may span across many medical, diagnostic fields; it is not the intention of the author to limit the scope of its utility. Focusing on visual impairment as it pertains to diabetic patients has been chosen merely to provide a manageable scope for this thesis.

II. DESCRIPTION OF THE ENVIRONMENT

A. ANATOMY OF THE EYE

The eye consists of three concentric layers of tissue enclosing the lens and other eyeball features. Figure 1 appears on the following page to illustrate the anatomical features of the eye. The outermost covering is comprised of the cornea and the tough, fibrous tissue called the sclera. The cornea is the outermost feature of the eyeball, hereafter referred to as the 'globe', visible as the transparent covering to the eye.

The next layer is the vascular layer of the eye responsible for the supply of blood to the outer layer of the retina. It includes the choroid, the iris, and ciliary body. The choroid extends from the optic nerve posteriorly and runs forward blending into the ciliary body and the iris.

The third and innermost layer of tissue is the retina. The retina covers the inner layer of the posterior two-thirds of the wall of the globe. It is the retina that receives visible light, analyzes the differing intensities, and sends this information to the brain for recognition.

B. DESCRIPTION OF THE RETINA

The principal landmarks of the retinal vasculature are illustrated and labeled in Figure 2. As can be seen, the retina is a very thin layer of tissue. It is merely 0.1 mm thick at the oro serrata, nearest the front of the eye, and 0.23 mm thick at the posterior pole. It is at its thinnest at the fovea centralis, situated in the middle of the macula. The fovea centralis is noted for its acute visual discrimination, which is due to the fact that the light receptors within this region of the globe are all cones.

Cones are the features within the eye responsible for picking out small, very detailed objects.

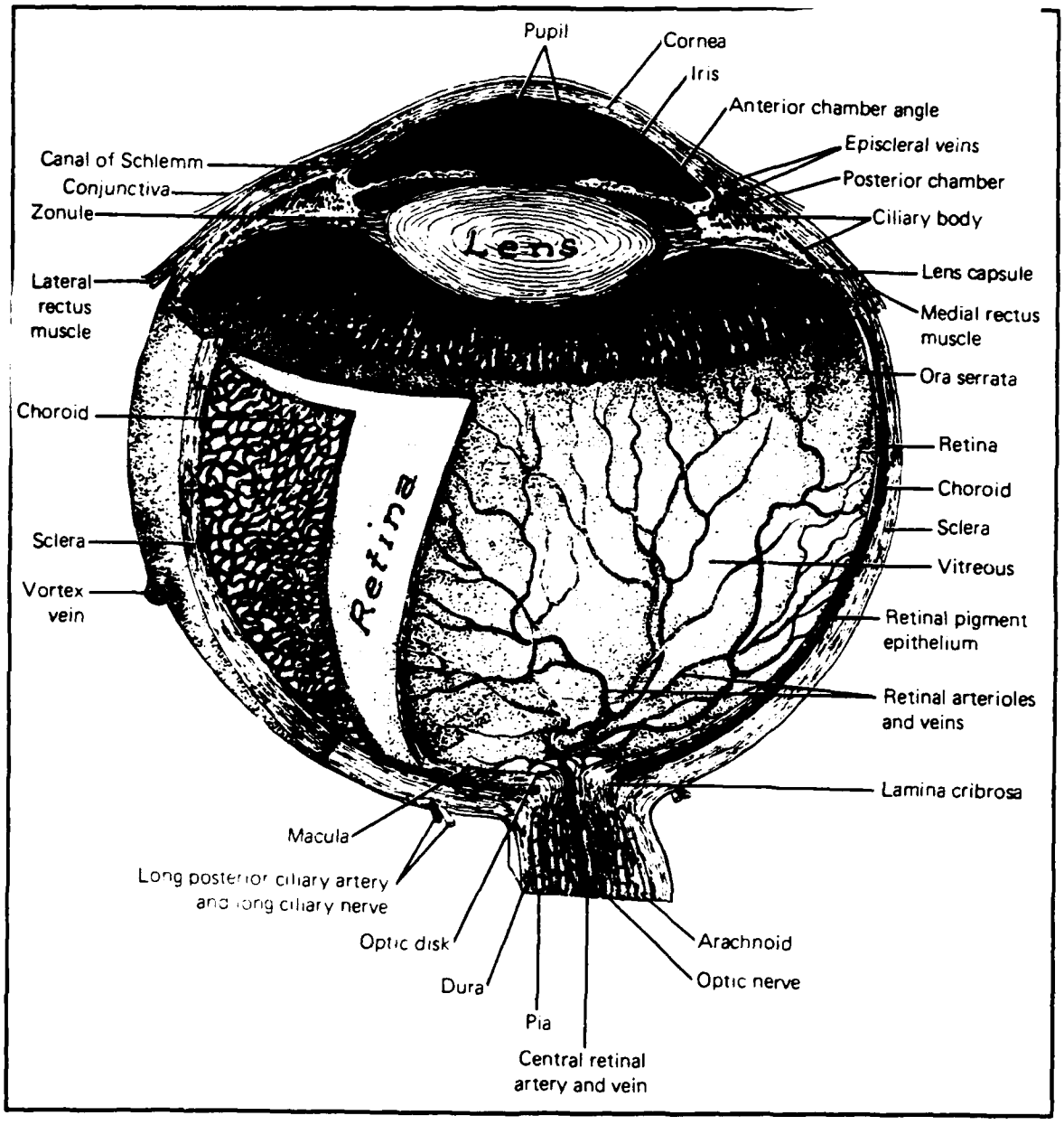


Figure 1. Internal Structures Of The Human Eye.
[Ref: Vaughan and Asbury, 1986, p. 3]

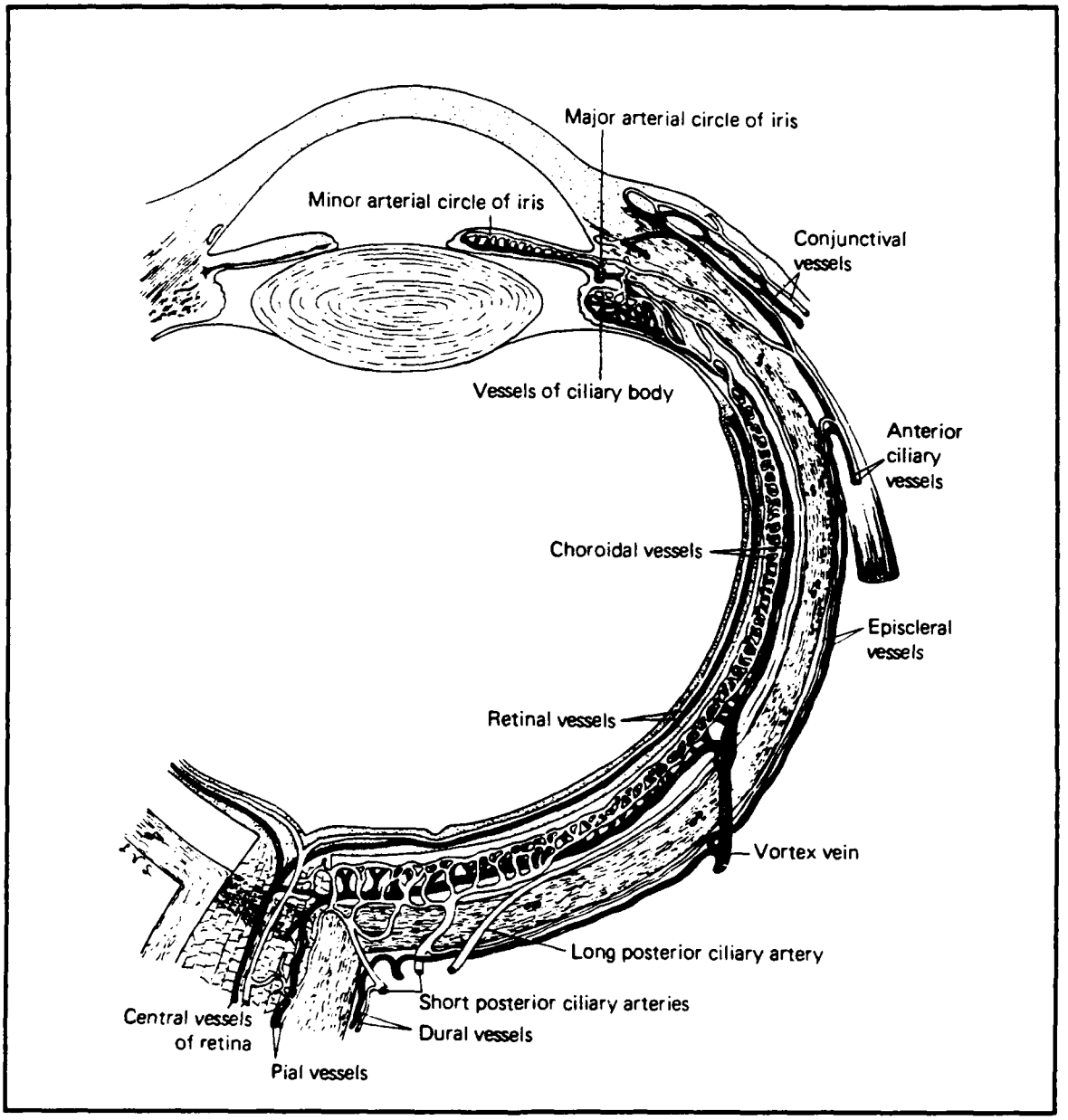


Figure 2. Vascular Supply To The Eye
[Ref: Vaughan and Asbury, 1986, p. 7]

Of primary importance to the retina's function, and to this study, is the source and flow of its blood supply. Figure 3 attempts to illustrate the features involved in the supply of blood to the eye.

The retina receives blood from two distinct sources. First, the choriocapillaris is a single layer of closely spaced capillaries attached to the outer surface of the basal (Bruch's) membrane, which forms a layer between the retinal tissue and the aqueous humor or fluid within the eye. Bruch's membrane lies immediately under the pigment epithelial layer of the retina. The choriocapillaris supplies the outer third of retinal vasculature.

Second, the inner two-thirds of the retina gets its blood supply directly from branches of the central retinal artery. Blood vessels run in the nerve fiber layer, and capillaries penetrate as deep as the inner nuclear layer. Considering the choriocapillaris is the only blood supply to the fovea centralis, this, the most important part of the retina, is susceptible to irreparable damage when the retina is detached and subsequent blood flow is cut off. [Vaughan and Asbury, 1986, p. 163]

C. TRACING THE CAUSES OF DIABETIC RETINOPATHY

Drs. Charles Garcia and Richard Ruiz, both of the University of Texas, Department of Opthalmology, trace four conditions which are believed to contribute to the state of retinal hypoxia (blood starvation), long regarded as the most logical factor in the cause of diabetic retinopathy. In the course of their study they documented the following five (5) conditions that have an effect to some extent on all patients suffering from diabetic retinopathy.

- Increase in Hemoglobin A1c Oxygen Affinity.
- Sorbitol Overload
- Changes in Blood Vessel Wall
- Changes in Blood Elements
- Vasogenic Factor [Garcia and Ruiz, 1984, p. 3]

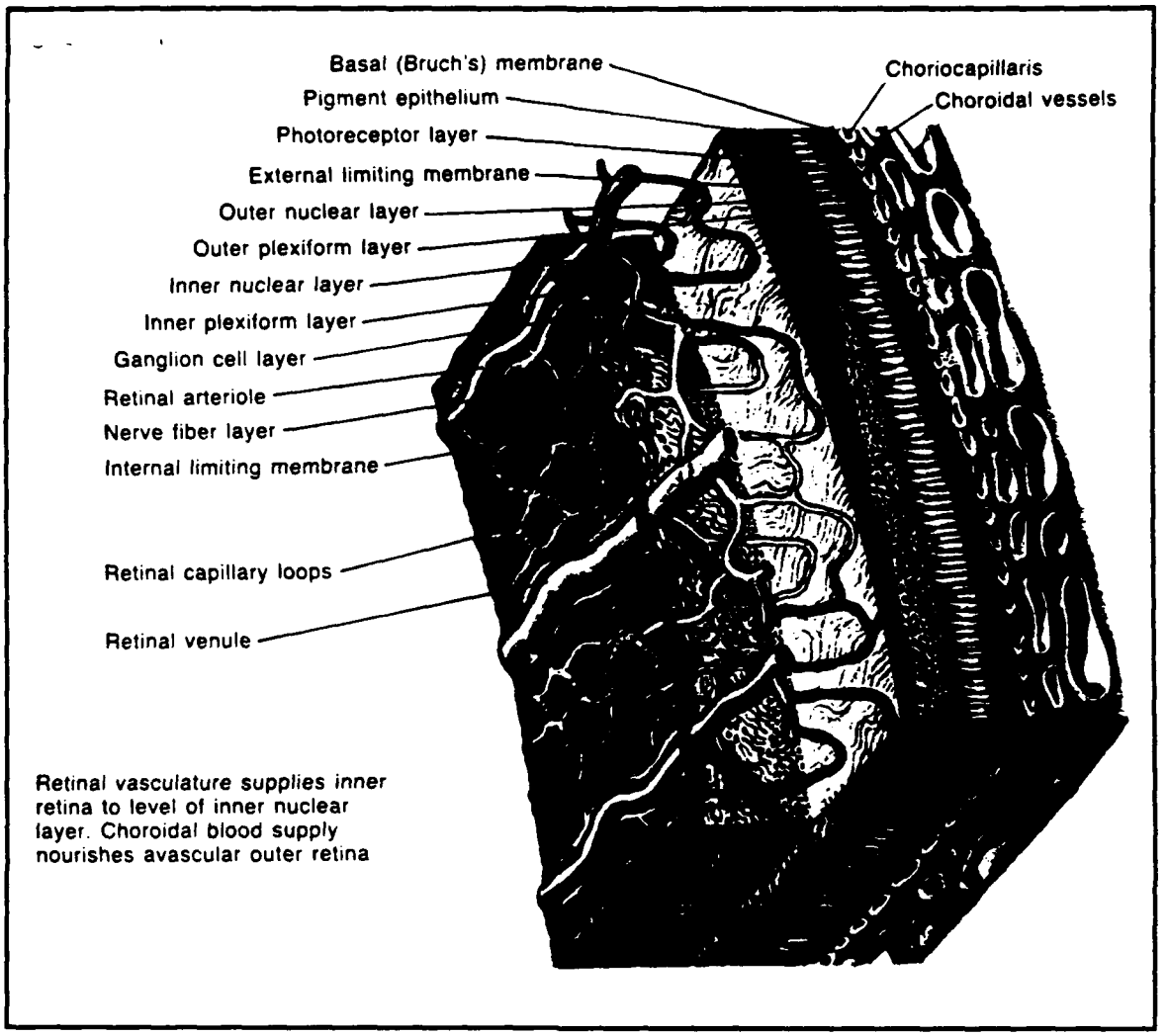


Figure 3. Retinal Blood Supply
[Ref: Garcia and Ruiz, 1984, p. 5]

Although a discussion of their causative factors is beyond the scope of this paper, their effects all combine in degrees to cause various adverse symptoms. Most notable among them is the onset of impaired autoregulatory blood flow. This impairment leads to subsequent abnormal conditions and eventual failure of the normal regulatory processes within the retina, leading to hypoxic states within the vasculature. Hypoxia, in turn, leads to a whole range of pathologic processes that are discussed in the next section regarding clinical findings.

D. CLINICAL FINDINGS

In the previous section the disruption of the normal regulatory processes within the retina were said to cause abnormalities. These irregular patterns cause tissue deformation that can be observed during the course of an opthalmoscopic examination. In addition, with the increased aid of fluorescein angiography, some of the more minute abnormalities can be readily observed with a subsequent diagnosis that more accurately reflects the situation at hand. A discussion of each pathologic change follows.

1. Microaneurysms

Microaneurysms are spot enlargements of the capillaries that appear as though growths are manifesting themselves. It is actually a weakening of the capillary wall that causes this dilated appearance. Typically from 15 to 50 microns in diameter, they may lead to further degeneration of the capillary vessels. Since a weakening and eventual rupture of the capillary wall is indicated, their diagnosis is critical while still in the early stages of presentation.

2. Hemorrhages

Hemorrhages in the middle retinal layers are usually seen as small, circular red spots with blurry borders. They result from leakage or rupture of the vessels. They are frequently described as dot-and-blot or flame-shaped, both of which may resorb in a matter of weeks. This finding, while rarely causing permanent damage, signals the onset of diabetes, hypertension, and conditions that slow venous blood flow.

3. Retinal Edema

Between the retinal cells there is a potential space that fills with fluid when the retinal capillaries leak. Blurred or lost vision usually occurs only when the

macula is affected by edema. One symptom is the rapid, temporary loss of visual acuity. This is a difficult diagnosis to make with the simple opthalmoscopic examination. Angiography alleviates the difficulty in properly diagnosing this finding because the fluorescein dye appears readily within the extracellular fluid after leaking from the normally impermeable vessels.

4. Hard and Soft Exudates

These exudates are lipoprotein deposits that form clusters around leaky vessels or microaneurysms. These deposits accumulate in middle retinal layers as a result of edema of long duration. They may persist for years and often resorb on their own when in the proximity of healthy capillaries. On examination they appear as spots in colors that vary from whitish-gray to yellow, depending upon their origin.

5. Other Findings

Additional findings include occluded arteries, neovascularization, fibrous proliferation, and traction retinal detachment. All play a part in the gradual decay of healthy blood flow and the impairment of vision. They are all visible upon an opthalmoscopic or angiographic examination.

While these findings may not be serious, in and of themselves; they do point to the possibility of more deleterious effects in the future. Timely, accurate diagnoses have the power to stem the tide of many of these embedded, harmful findings and their associated diseases. That's why it is critical to discover and treat such diseases in their infancy. Given a precise, diagnostic tool to probe beyond the surface, where abnormalities are known to develop, medical specialists can get an earlier start on the treatment of this disease.

E. DIABETIC RETINOPATHY

Diabetic retinopathy is one of the leading causes of blindness in the Western world. Its frequency increases with the length of time diabetes is apparent in any patient. Research conducted in recent years has suggested a direct correlation between poor antecedent blood glucose control and increased incidence and severity of retinopathy [Vaughan and Asbury, 1986, p. 167]. It is this poor glucose control within the blood that is the major contributing factor of diabetes mellitus.

The normal progression of retinopathy is divided into a preclinical stage and a clinical stage. In the preclinical stage, special diagnostic techniques may or may not discover the pathological changes that are the precursors to the findings described in the previous section. A routine opthalmoscopic examination may completely overlook some of these minute changes, often developing in the underlying tissue, beyond the view of the unaided eye. Some telltale signs in this stage include increased retinal blood flow and a gradual thickening of the basement membrane [Garcia and Ruiz, 1984, p. 14]. It can therefore be supposed that a diagnostic tool which could investigate beneath the surface layers of tissue would have a profound effect on discovering these early symptoms.

The clinical stage, with its increasingly visible characteristics, is broken into two distinct phases, background or non-proliferative diabetic retinopathy and proliferative diabetic retinopathy.

1. Background Diabetic Retinopathy

This phase is typically the first recognizable retinal pathologic finding. Characteristic clinical findings include microaneurysms, dot-and-blot hemorrhages, hard exudates, and focal areas of capillary expansion or enlargement. Background retinopathy usually progresses slowly, and visual loss is rare. It is only

in the cases where maculopathy presents itself that visual loss is even possible. Maculopathy refers to the visual loss caused by edema, hemorrhage, vascular occlusions or exudates involving the macula. [Garcia and Ruiz, 1984, p. 15]

The prognosis for patients with background diabetic retinopathy is good, with only 3% of patients becoming blind within five years. Macular edema is the common cause of impaired visual acuity in this phase. In background diabetic retinopathy, attention is focused on optimizing control of blood glucose and hypertension. If diagnosed early and accurately, the symptoms may, in some patients, disappear altogether.

2. Proliferative Diabetic Retinopathy

The most severe complications involving the eyesight of diabetic patients are associated with the proliferative phase. Most of the symptoms of the background phase are still present, but are more pronounced. Additionally, entirely new blood vessels called neovascularization appear, often developing in as little time as two weeks. These new vessels multiply and then start to actually grow away from the retina, pulling it inward causing detachment if left unattended. If the vessels bleed, massive hemorrhages may cause sudden vision loss. In the case of sudden, painless loss of vision, it is practically always due to an occlusion of the central retinal artery or an occlusion of the central retinal vein. [Gordon, 1962, p.139]

Although proliferative diabetic retinopathy typically develops over a number of years, it may progress extremely quickly in some patients. Patients at greatest risk are those under 30 years of age with either undiagnosed or poorly controlled diabetes. In most medical opinions, the importance of early detection and regular monitoring cannot be overemphasized in controlling the effects of

proliferative retinopathy [Vaughan and Asbury, 1986, p. 169]. Such careful measures can stem the tide of vision loss for a great percentage of these patients.

F. EXISTING DIAGNOSTIC TOOLS

There are numerous instruments, methods, and procedures in use today that aid in the diagnosis and treatment of eye disorders. These tools, in turn, provide the medical specialists with avenues to explore further into the causes and development of related diseases. Some of these methods have been in use for several years. For example, the common opthalmoscope has been in continuous use for over 135 years.

It is imperative that new techniques and ideas be explored, for without fresh thought some of the devices to be described in the following section would never have come to fruition. Each tool has developed its own particular niche in the process of diagnosing disorders. Each performs its task well, yet the question must always be asked; is it good enough?

Two methods of retinal imaging will be discussed: opthalmoscopy and fluorescein angiography. While there exist numerous methods beyond these to provide detailed eye images to medical specialists, these two enjoy the most frequent use by all diagnostic fields involved in the diagnosis and treatment of diabetic retinopathy. They represent both the old and the new in discovering and treating the disabling effects associated with this disease.

1. Opthalmoscopy

In 1851 a German physicist, Herman von Helmholtz, invented the first opthalmoscope. It is obvious, by the fact that this instrument is still in extensive use today, that this invention is an enduring, valuable instrument in the ongoing diagnosis and treatment of eye disorders. Properly trained specialists, through the

use of this device, are allowed a view like no other afforded anywhere else in our bodies, namely that of vascular and nerve tissue without the disturbing intrusion brought on by surgical procedures.

The extraordinary view provided by the opthalmoscope remains an integral part of the most common physical examinations, not just those of eye specialists. With its wide use, many irregularities are found during the course of these routine examinations with subsequent referrals to eye care specialists in the hope of avoiding further problems.

There are two types of opthalmoscopy: 1) direct and, 2) indirect. Each provides the specialist with valuable insight into distinctive clinical findings. Both direct and indirect opthalmoscopy are used in specific circumstances when conditions warrant the use of one over the other. These conditions will be explained on the following page.

a. Direct Opthalmoscopy

Direct opthalmoscopy makes use of a small but strong beam of light that is directed onto the patient's eye with the use of a mirror within the opthalmoscope. This incident light is then reflected from the fundus of the patient's eye through an aperture located in the center of the reflecting mirror. In this way the specialist can view the unaltered image of the patient's eye. An illuatration of direct opthalmoscopy is provided by Figure 4 on the next page.

The aperture is to be held as close to the patient's eye as possible. The proximity to the patient's eye facilitates focusing the image of the inner eye. Should a suitable image with clear features be impaired, several lenses are typically available within the instrument to remedy this problem.

A typical examination with this instrument includes an inspection of the retina, retinal blood vessels, macula, optic disk, choroid and sclera. Direct opthalmoscopy holds a great utility for eye specialists because a wide region within the eye can be readily viewed. For example, the retina can be examined as far anteriorly as the equator if the patient's pupils are dilated fully. The instrument is also quite portable and, with a proper amount of training, can be mastered quite handily. It is a widely used, relatively inexpensive diagnostic tool that provides a simple, accessible method of detecting eye problems.

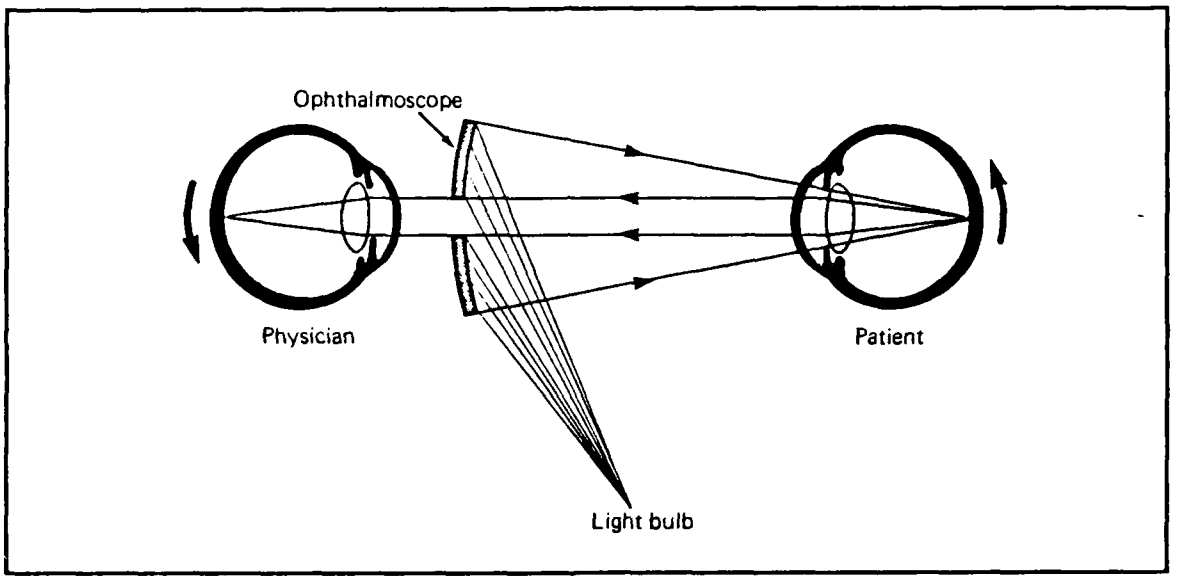


Figure 4. Direct Opthalmoscopy.
[Ref: Vaughan and Asbury, 1986, p. 35]

The drawback to this method is that if the specialist does not perform the examination in a careful, methodical way some smaller, less obvious abnormalities may inadvertently go undetected and no permanent image remains to allow later, in-depth study. In view of this, direct opthalmoscopy is extremely reliant on the expertise and recognition capability of the user. In addition, the fundus image cannot be greatly enlarged. There are a multitude of features the

well-trained specialist can detect without several powers of magnification. Unfortunately, minute conditions do periodically go unnoticed, particularly if they are not prolific and especially if they exist below the surface of the choroid.

b. Indirect Opthalmoscopy

Another tool for imaging the inner eye is indirect opthalmoscopy. This instrument, similar in operation to the direct opthalmoscope, includes the use of an additional convex lens in line with the returned image. A depiction is provided in Figure 5. By so doing, a larger field of view can be readily observed. Additionally, with the aid of the extra lens, refractive errors that would otherwise cause distortion of the patient's fundus are avoided. The disadvantages to this method are that a reasonable power of magnification is not provided, the pupil must be dilated and, because of the convex lens, all images are inverted. This last disadvantage is a potential source of confusion or misunderstanding if not handled meticulously.

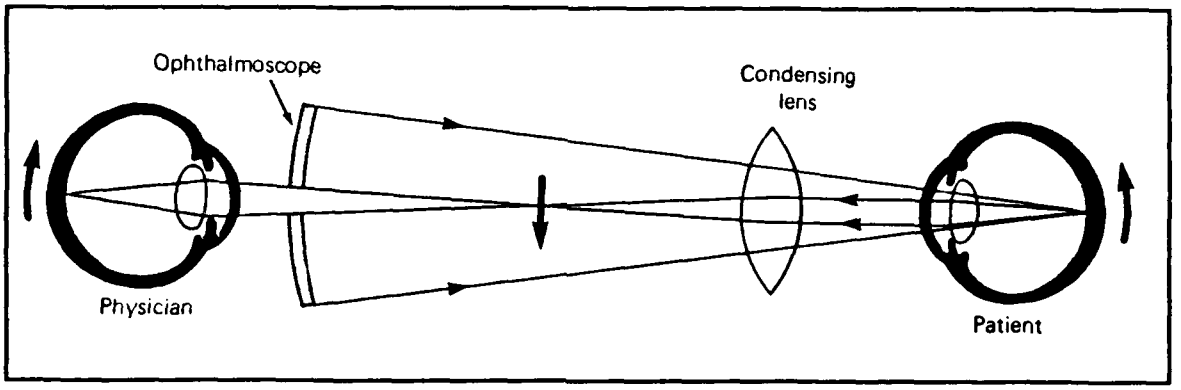


Figure 5. Indirect Opthalmoscopy
[Ref: Vaughan and Asbury, 1986, p. 35]

2. Fluorescein Angiography

Fluorescein angiography is a relatively new opthalmologic method to view the vasculature within the eye. It uses a fluorescein dye to naturally highlight the

vessels contained by the retina and choroid and then further uses normal photographic means to retain a permanent image. In recent years it has risen to a level of great diagnostic importance and enjoys widespread usage in the field of opthalmology and, more specifically, in the diagnosis of diabetic retinopathy.

The procedure begins with the dilation of the patient's pupil to the maximum extent possible (maximum mydriasis). Following this an aqueous sodium fluorescein is rapidly injected into the patient's arm (antecubital vein) with them in a sitting position, positioned in front of a fundus camera. Black and white photographs are then taken with the aid of the fundus camera equipped with an automatic advance and a high-intensity flash. For purposes of comparison, nominal photographs are taken prior to the fluorescein injection. Thereafter photographs are taken in rapid succession at half-second intervals for 20 seconds. If additional exposures are warranted, the attending specialist can take them up to 5 minutes after the injection and still get some residual highlighting effect on the fundus from the dye. Also, if desired, normal indirect opthalmoscopic methods can be used to facilitate the residual effects of the fluorescein injection for diagnostic purposes.

The normal procedure of fluorescein angiography can be divided into three phases:

- Filling Phase
- Recirculation Phase
- Late Phase

a. Filling Phase

The filling phase typically lasts 8 to 20 seconds beginning at the injection. It is at this point that the choroidal circulation shows the first telltale signs of the fluorescence, preceding retinal arterial filling. The effect is first seen in the macular area and then spreads outward toward the periphery. If there are

problems, the fluorescein will now leak from the choroidal vessels to the extravascular space.

The retinal arterial filling starts approximately one half-second after choroidal circulation. Following this is a period in which the capillaries fluoresce and then there appears a venous drainage phase.

The retinal pigment epithelium acts a a physical barrier to the injected fluorescein. It prevents leakage of the dye into the inner retina and, except in albino patients, masks most of the fluorescence of the underlying choroidal circulation. It is therefore ineffective in this area of the retina.

b. Recirculation Phase

The recirculation phase lasts approximately three to five minutes after completion of the filling phase. It is at this time that the fluorescein concentration in the choroidal intravascular and, if there are abnormalities, extravascular spaces is equal. In an unaffected retina, one devoid of leaks, hemorrhaging, and other abnormal findings described previously, fluorescein is confined to the intravascular space and there is no obvious leakage to surrounding tissue and vitreous.

c. Late Phase

The late phase occurs about thirty to sixty minutes after the initial injection. During the late phase, there remains little or no fluorescein of much practical use in the retinal vessels. There may be a very faint staining left in the choroid but the levels are of little assistance in any accurate diagnoses. This stage marks the natural elimination of fluorescein from the body.

III. METHODOLOGY

A. FINDING THE RIGHT PEOPLE

Considering the availability of the technology contained by the Eye-Dentify system, described later in the study, and, with some knowledgeable input from a large laser manufacturing company, it was postulated that an expanded system for use in a medical application is possible. It was with this in mind that two leading medical specialists from the Monterey area were contacted and asked their opinion on the utility of a system suited to their purpose. The doctors polled were Dr. Eric J. Delpiero, an ophthalmologist/retinal & vitreous specialist from Monterey, California and, Dr. Curtis Javorsky, an endocrinologist working in Watsonville, California. How they arrived at being the chosen specialists to render opinions on the concept will be explained later. Beside their comment on the concept itself, these specialists were also approached with the premise that they assist in the preliminary design by suggesting possible functions they would personally prefer if such a system were available at present.

The specifications found in the following chapter are the result of that effort. The functional specifications were arrived at with input not only from the two medical specialists, but also with the combined expertise of laser and computer experts. It was noted that the doctors, by maintaining currency and the demands of their own specialties, were not fully aware of the latest technological strides in both the computer and laser fields. In this regard, the author used a variety of sources in the drafting the complete list of specifications. By tendering the medical input,

listening to their existing needs as well as future desires, and then validating this with the technology, the total system concept was carefully blended and shaped.

In addition to the two local specialists, the concept was initially presented to both the President and the Chief of Scientific and Medical of the American Diabetes Association. Their responses and opinions, while not responsible for specific guidance, are duly reflected in the general tone of this study and their interest, greatly appreciated, has opened doors that might otherwise have remained closed.

B. THESIS CHRONOLOGY

The study was formally started in May of 1988. It was through an introduction from personal acquaintances, two nurses in the San Francisco area, that Dr. Charles M. Clark, Jr., President of the American Diabetes Association (ADA), was initially informed of the concept. Donna Mapes, RN and Martha Price, RN, D.N.Sc., then working on a cancer study, provided an introduction to several doctors that were interested in the preliminary design features of the automated scanning system as they relayed them. Through continuing correspondence to the Indiana University School of Medicine, where Dr. Price now resides, the ideas for the concept were discussed with several of the Medical School staff. Modifications and tailoring of the proposed system were the main topic. It was at this time that the comment was made that a system such as this might have the potential to possibly replace the existing slide photography of retinal fields. It was stated that the current methods were time-consuming and uncomfortable for both doctor and patient alike. An interest was expressed by the staff at Indiana University as to whether this system could provide equal or better retinal imaging. During the months of June and July further inquiries into the technological viability and medical applicability of this system were in progress.

In August of 1988, Dr. Clark responded by letter stating that the concept of automated imaging and retinal comparison "would be an excellent concept." Apparently he had had conducted some discussions with the other staff members aware of the concept and felt it was a good idea, although he expressed some misgivings about the technological limitations that might be involved. Further, it was his expressed wish that contact be made with the National Headquarters of the ADA with information regarding the concept.

In early September a phone call was placed to Richard Kahn, PhD., the Chief of Scientific and Medical of the ADA. A meeting was arranged and the latest ideas and proposed features for the concept were presented. From that discussion, it was affirmed that: 1) no similar projects were currently known by the ADA to be either in development or use and 2) the process of retinal imaging had yet to advance beyond visible spectrum (photographic) methods. It was his suggestion that I contact Dan Snare, the head of the California Affiliate of the ADA, to begin the process of formally researching the concept and to enlist the assistance of some local medical specialists involved in the fight against diabetic retinopathy. Mr. Snare referred me to Dr. Javorski of Watsonville, a community close to Monterey, who is affiliated with the ADA. The remaining doctor asked for specific comment, referred by Dr. Javorski, was Dr. Eric DelPiero of Monterey.

During the months of October and November, these two noted, highly professional specialists were presented with a brief overview of the current state-of-the-art in both computer and laser technology as they applied to this concept. At the completion of the presentation they were asked to complete a survey form, outlined in the Appendix, describing their opinion of the concept as presented, as well as to list some features they felt would make the system of more practical, productive use

to themselves. It was through these surveys, and the discussions that ensued, that some of the functional specifications were drafted.

C. REASONING FOR THIS APPROACH

The primary assumption in researching this proposed system has always been that the ultimate users of this system, the doctors, must be granted an important say in the preliminary design. It is hoped that by allowing these medical specialists to play a key part at such an early stage that not only would the system gain some reputability among those reviewing the earlier prototypes, it would also return a benefit by establishing the system as a practical, productive device from the very outset.

This strategy is deemed necessary not only for the sakes of reputability and practicality but also to later assist in bringing the system to production. It is submitted from experience that large-scale projects are frequently subject to production delays and expensive post-design modifications because sufficient, early attention was never paid to the ultimate users and beneficiaries of the very system proposed. By giving a voice to the people that will be involved in this system's use on a daily basis, it can be inferred that not only will a more useful product be delivered, but perhaps it can be delivered quicker and cheaper.

IV. FUNCTIONAL SPECIFICATIONS

The idea for this thesis was borne out of numerous discussions the author initiated with several medical specialists from across the country. It became apparent from these talks that there exists a need for further development and refinement of the vascular imaging process. This is not to say that current methods are lacking; they are not. They provide valuable, necessary insight, however, the doctors that were contacted stated that not only would automating the process allow greater accuracy in their diagnoses, it could also conceivably lead to the testing of several theories that now go unproven because of their need for extreme accuracy in the mapping of the vasculature and its underlying tissue. Methods such as angiography and opthalmoscopy cannot provide for either the accuracy or detail required to assist in testing these new theories. Principally, the primary purpose of this proposed system will be to improve upon the current method of retinal imaging.

It was stated in an earlier chapter that fluorescein angiography is currently the most widespread method of viewing the retina. However, from the start of the process it often takes up to a half hour before the doctor can view the prints from this photographic process. Another factor to be considered is the time required of the patient to remain perfectly still. Patients must remain motionless, without blinking, while the opthalmologist takes up to 36 continuous exposures with a fundus camera. Normally several exposures are unusable because the patient blinks or moves, blurring the photograph. Lastly, the amount of detail and diagnostic use that comes from these photographs can most definitely be improved, simply with existing technology drawn from off-the-shelf components.

A. IMPROVING UPON THE EXISTING TECHNOLOGY

It has been proven by the Eye-Dentify Company of Portland, Oregon that small areas of the retina can be digitized and read into a computer for use in the indentification of personnel. This system of identification is required by organizations, largely the government, that have a need for such a security device. Through the use of precise optics to read the vascular pattern and a computer that transforms the data to a usable format, the Eye-Dentification System 7.5 is able to image a small portion of an individual's retinal pattern and distinguish it from any other that may be resident within the computer's memory. Considering the vascular pattern contained in each person's retina is singularly unique, the system guarantees virtually perfect reliability in the identification of assigned personnel. The company's advertised false acceptance rate is one in one trillion. [Eye-Dentify Inc., 1988, p. I-3]

The Eye-Dentify system works as follows. It uses an ultra-low intensity, infrared light source (not a laser) to scan a circular area of the retina, approximately 7 mm in width. The approximate size of the scanned area is illustrated by Figure 6 on the following page.

Once the scanner completes its task, it then creates a digitized waveform that is relayed to a 68000 microprocessor where it is processed, used to identify the user, and then stored in memory for later use [Eye-Dentify Inc., 1988, I-3]. The system uses a bubble memory to retrieve and sort needed retinal patterns and has the capacity to hold 1200 individual templates within the unit itself (stand-alone configuration). By attaching a personal computer, the system's capabilities are expanded and the process of imaging the retina sped up.

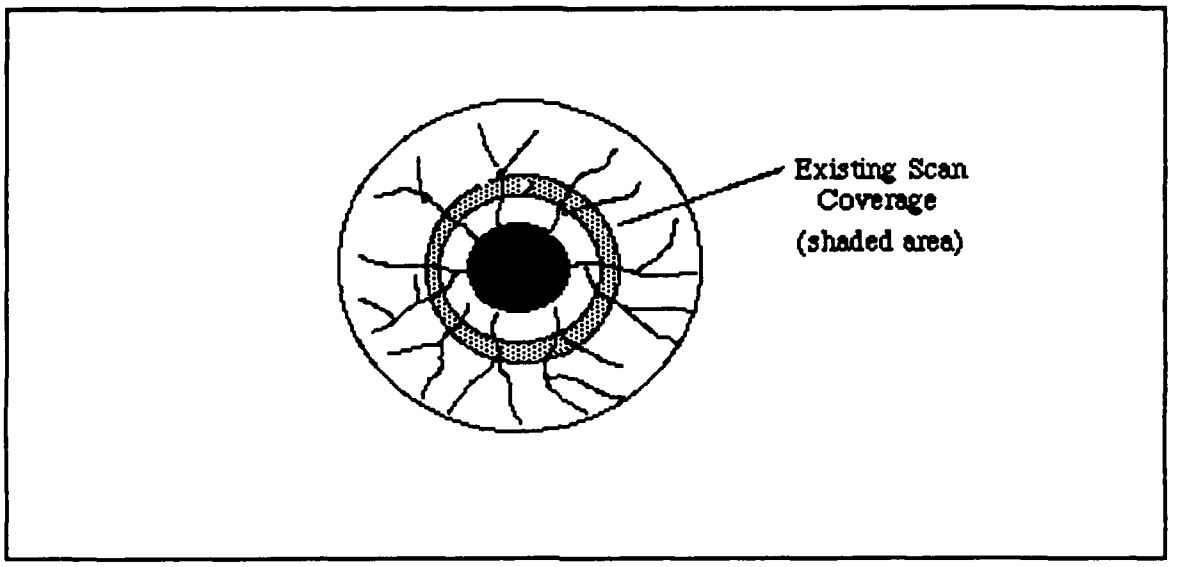


Figure 6. Dimensions of the Eye-Dentify Scan

In an independent testing of the system for the government, Sandia National Laboratories of Albuquerque, New Mexico verified that the entire image uses only 40 bytes per individual pattern and, on average, takes only 7.5 seconds to identify the subject [Sandia National Laboratories, 1987, p. 4]. With the amount of testing that this system has undergone from several independent laboratories, it is plain to see that it is a reliable, accurate technology.

The remaining portion of this chapter will deal with describing the sub-systems contained by the total concept and the specific performance requirements that will render the system usable in its intended medical application. For ease of explanation, the system will be divided into a computer sub-system and a scanner sub-system. Each section presents its own particular issues and, when pieced together will comprise the comprehensive performance characteristics felt necessary to continue with the further development of the system.

B. SPECIFICATIONS TO THE SCANNING SUB-SYSTEM

While the doctors and other ultimate users of the system might state that the graphic interface is the most important sub-system of the entire concept, it is the author's estimation that the scanner that holds that honor. Without a suitable scanner no data would reach the CPU for processing and the image would not be possible at all. This is the most critical part of the system and the part that will require the most forethought in both design and integration to the whole.

The functional specifications delineated below were formed under the assumption that the technology to support these specifications exists. In fact, the technology does exist to reach into the eye returning usable data while causing no harm whatsoever to the eye. What is yet untested is the manner in which images are returned to a screen for viewing.

It is a laser, and not simply an infrared light source, that has been researched for this early stage as the best available scanning medium . The resolution and focusing capabilities it provides as well as its ability to penetrate many substances, both liquid and solid, make it a clear choice over infrared light for use in diseased eyes. With the many abnormalities that exist within the eyes of diabetic patients, and looking further, to those of progressed opthalmologic patients, the laser, in whatever form chosen meets the preliminary requirements of this proposed system.

1. Size of Characteristics To Be Detected

In this regard, Dr. DelPiero, a retinal and vitreous specialist, stated that the size of the smallest abnormalities currently searched for are approximately 5-10 microns in size. The opthalmologists involved with the study believe that a system that provides more detail might be helpful, but the common clinical findings all

present themselves minimally in the sizes listed above. Lasers are known to discriminate features down to 1 micron in size.

2. Desired Scan Coverage

To suit the purposes of most all opthalmologic and diabetic diagnoses, a conical area bounded by approximately 60 degrees, or 30 degrees from centerline, is required for a medically viable scan. A predominate portion of all eye features as well as all of the retinal vasculature is contained within this area. A depiction is found below in Figure 7 to illustrate this.

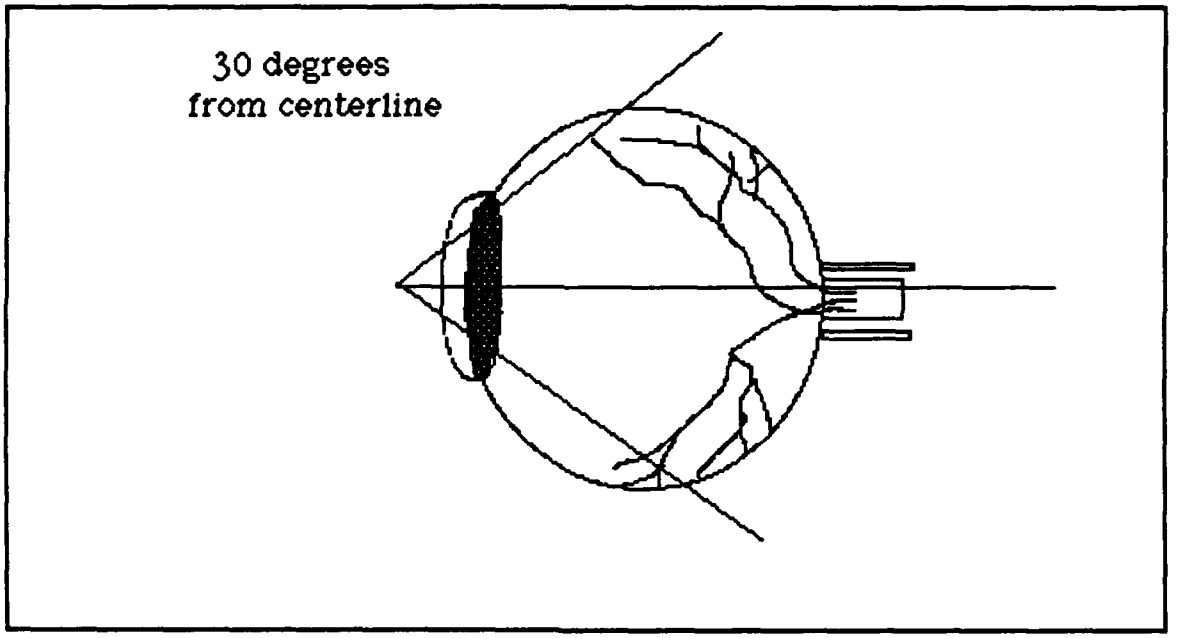


Figure 7. Area of Proposed Scan Coverage

Relying on the medical specialists to state what their need is for this size of an area, they feel that to be of practical use the scanner should reach the full area of fluorescence, or that which is normally highlighted by fluorescein angiography. There are long-held procedures and diagnostic measures to properly diagnose this

specific portion of the eye and initially it would be wise to facilitate their time-worn experience and proven procedures.

3. Tissue/Vitreous Penetration Requirements

Opthalmologists claim that a system that could return an image showing abnormalities below the vascular layer, or sub-choroidal, would be revolutionary. There is no system in use today that can perform such a feat. It was commented that retinal specialists need a system that would be able to view below the surface of the retina to determine the depth of lesions and the extent to which they are resident. By determining what is occurring at a distance below the choroid, it may be possible to detect diabetes earlier and stem the tide of retinopathy in those patients so afflicted. Additionally, retinal specialists would take delight in exploring below the choroid in treating many other eye afflictions since they currently have no means to explore visually to any significant depth.

Another consideration would be the penetration of a cloudy lens as well as other vision-impairing abnormalities sometimes found within the vitreous (fluid) of the eye. To counteract these impairments the laser would have to be able to alter its frequency of emitted light in order to achieve penetration of these substances. It would require it to be frequency-agile. This would demand that a utility be built into the system that would either manually or automatically sense that a blockage of light is occurring and a resultant frequency change is warranted. Other characteristics to be accounted for would be the refraction of the laser beam as well as the opacities of all manner of resident abnormalities within the eye.

In selecting a laser for the scanning sub-system it may be possible to"see" through many of these obstructions and reach into the choroid to provide the specialists with the needed information. Currently some lasers can penetrate up to 2

millimeters below the skin of subjects. The depth of penetration in softer tissue is as yet unknown. It will be a significant technological feat to provide all that the opthalmologists hope for with this system.

4. Communication With the CPU

It will be imperative for the scanning sub-system to communicate reliably and quickly with the computer sub-system. To this end, the data sensed by the scanner should be formatted in such a way that the processor can transform this information into a well-detailed image, suitable to diagnostic need. It could be any one of a number of commonly used byte translation schemes, for example, hex-ASCII format. Regardless of the method that is subsequently chosen, it should be that which best renders a detailed, coherent image and offers the most capability in the manipulation of this data to enhance the image on-screen.

B. SPECIFICATIONS TO THE COMPUTER SUB-SYSTEM

The requirements that are proposed for the computer sub-system will be defined within this section . There will be principally two pieces of hardware comprising this portion of the total system 1) a microcomputer, or central processing unit (CPU) to facilitate the transformation and storage of the data from the sensor/scanner into a computer format and, 2) a monitor for viewing the specified area of the retina.

A microcomputer has been chosen as the model for this study because, when one considers the ever-increasing power and ability of these smaller devices, it is easy to find a computer of this size to perform all the needed functions of this proposed system. To prove this, the Eye-Dentify scanning system does not even require a separate, attached computer to perform its function. All the computational and storage power it needs is contained within a single, stand-alone

unit that is capable of handling 1200 unique eye patterns. However, with the requisite increase in the size of the scanned area needed by the proposed system, an attached microcomputer is a necessity. To assist in conceptualizing the system as it may appear, an illustration of the proposed, complete system is provided below in Figure 8.

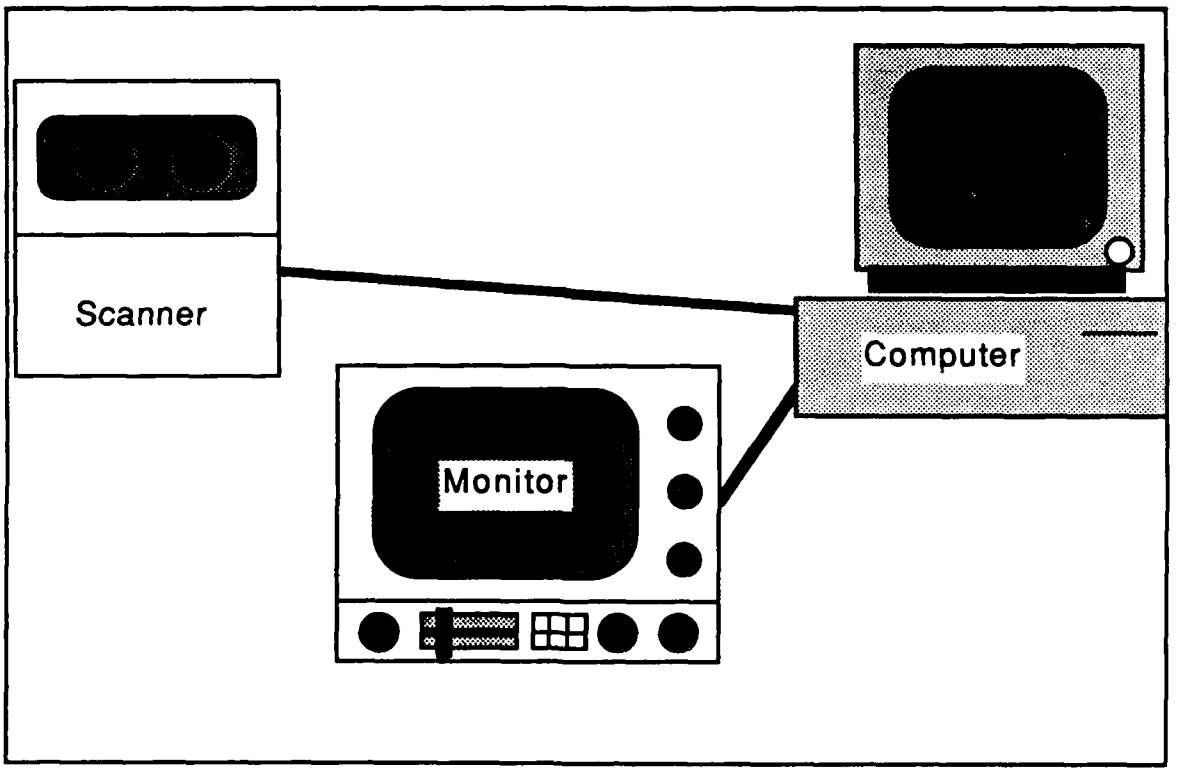


Figure 8. Conceptualized Drawing of the Imaging System

1. Memory

The amount of expandable memory available to the system and its proper utilization is an important issue but is foreseen as one with an easy remedy. Today, with the increasing availability and cheaper costs of mass storage units, hard disks, the only limit to the user's ability to store eye patterns will be how much they can afford to spend on their particular system.

To illustrate the amount of memory needed by any one user it is best to use an example of a system already in operation. The Eye-Dentify system described earlier uses a mere 40 bytes of internal memory for each eye signature. Considering this, if the Eye-Dentify system is provided with just a modest 20-megabyte hard disk, well over 500,000 individual eye patterns can be stored and made available for immediate use. Realistically, however, with the size of the scanned area in the proposed system obviously in need of much more than 40 bytes, the total amount of stored retinal patterns will diminish, yet not so much as to offset the benefit gained by the availability of the expandable memory.

a. Estimating The Need For Memory

In arriving at an estimate for a baseline system configuration for the proposed system, the doctors surveyed were asked to estimate the number of patients, frequency of visits, and number of retinal images needed by their patients in one year. The doctors in the two specialties gave different estimates. Currently, the opthalmologist reported seeing 5,000 patients per year with a need for approximately 10 images per visit. Included in this figure are patients with all manner of diseases, not solely diabetes. The endocrinologist, with a more specific range of patient diseases seen and, with just a portion of them needing diagnoses based upon examinations of the eye, returned a yearly figure of 500 patients. They also estimated approximately the same amount of images taken per visit.

Both doctors agreed that their need for memory would probably increase proportionately with the perceived utility of the system. Based upon their estimates, the range of eye patterns to be taken in any one year is from a low of 5,000 for the endocrinologists to a high of 50,000 for the opthalmologists. Given

the amount of storage space required of each retinal image, the medical specialists can then knowledgeably make the choice of how large a memory unit they need.

b. Managing The Storage of Retinal Images

Relatively easy storage and retrieval of the eye patterns will also be a necessary feature of the memory. It should be accomplished through the use of any number of database methods developed and currently available on the market. This image management scheme will have to account for each eye pattern so asto allow classification and identification of the images and allow the user to attribute these images to a specific patient, disease, or through whatever means the user chooses for his own benefit.

With the proper image management scheme and a suitable amount of available storage space, the complete system will be greatly enhanced and of much benefit to the diagnostician. When presented with the decision of what configuration is needed, each doctor can review his past patient load and estimate his configuration requirements; size of memory and database method to be used. In turn he can make the choice of what unique components will support his specific needs. The true utility of the system will be, irrespective of the accuracy of his numbers or the estimation of his level of use of the system, that a modification is possible with no alteration to the basic operating components. A mere component-part addition or deletion can be made at his convenience.

2. Graphic Interface

The graphic interface may well be the heart of the entire system from the doctor's perspective. From the images to be displayed on the screen, the doctors will make their diagnoses and help treat the manifold diseases afflicting their patients. While interviewing the specialists for this study, it was here that the

medical specialists were most interested in lending their opinion to tailor a system of graphic representation that will be of use to their work.

Their ideas and suggestions were heavily weighted for their expert opinions and experience, not only with the patients they see, but with the current imaging methods they have to work with daily. In the many discussions that transpired, these specialists had very specific comments and requirements of a system to improve the way they conduct their practices. What follows below is a mixture of specifications suggested by both the author and the three local doctors polled. Once the doctors were presented with what was feasible using modern technology, they then rendered their opinions as to what would make this system work best for them.

a. Enlargement Feature

On-demand area enlargement is a highly preferable, almost *mandatory feature. It would allow close-in viewing of specified areas of the retina.* In this way, trouble spots that may be particularly difficult to view with other methods may appear much larger than life-size with increased detail.

b. Template Overlays

This feature would work best in comparing past eye images with newer ones. This feature would give the specialist the capability to overlay extremely accurate images of the patient's retina and allow him to confidently make observations regarding the changes in a particular patient's diagnosis. Additionally, by carefully observing the effect particular drugs have on the diabetic's vasculature, dosages can subsequently be modified or changed altogether before lasting damage to eyesight might occur. This is particularly significant because the drugs normally used to combat diabetes have a profound, adverse effect on some patients.

Occasionally, while attempting to treat their retinopathy, in fact, the patients' problem with vision is worsened. The uniform concern from the doctors is the rapid identification of these patients through the use of a system that can render a quick, accurate estimate of the effect the drugs have.

Given the level of computer accuracy that will be utilized along with a uniform scale in the size of these eye templates, a new groundwork can be laid for comparative testing of the eye patterns. To this point, considering the inherent inaccuracies of the photographic methods currently used, no such capability approaching the accuracy of the computer exists to allow such a process of comparison.

c. Automated Template Comparison

Adding to the utility of on-screen template comparison would be the feature of automating this overlay process. By stating specific parametric limits, any blood vessels or other feature within the eye can be marked by the computer if measured outside of these stated limits. By so doing, a greater probability of finding minute abnormalities can be interjected across the entire field of diabetic retinopathic diagnosis. It would still allow the doctor the opportunity to make his learned decisions while taking the drudgery out of the procedure of simply finding these abnormalities .

If this feature could be made readily available, the computer, again, would enhance the possibility of not only finding hard to see imperfections, but would also assist in determining exactly when they first occur and their relative sizes. No such method of automated comparison currently exists.

d. Monitor

A recommended baseline size for a monitor is 10 inches. This large a screen would provide the specialists with a moderately-sized area for viewing even the smallest eye features and abnormalities while allowing some space along the periphery for system control windows. In defining a viewing sub-system that utilizes the full potential of the complete system, both doctors expressed the desire for a color system to accentuate the differences among the internal eye features as best as possible. Further, it was presented, and they agreed, that it would be most beneficial to allow the diagnostician the ability to change or designate colors of specific features to aid in the diagnoses.

e. Accessibility Of Controls For The System

A concensus was reached among the two principal doctors surveyed and other doctors presented with the concept; that was to ensure that the capability exists to keep button pushing to a minimum during repetitive imaging procedures. The medical specialists all expressed a disdain for long, involved control procedures to return images. Although some would like the ability to use the more elegant, laborious utilities that may exist in the system, even these people expressed the opinion that the normal processes be kept moderately simple. In this regard, it can be recommended that a mouse control for the system be provided, with a keyboard accessible only for text entry and as an alternate control method. User-friendly is the operative word and a system of control, such as Apple Computers use with their Macintosh, would be most preferable.

V. CONCLUSIONS

As this study concludes, a review of what it has proposed for use today and what it hopes to accomplish in the future is in order. As aids to the medical community, both opthalmoscopy and angiography will continue to provide quick, uncomplicated assistance in the diagnosis of diabetic retinopathy. Their past contribution as well as their enduring utility will guarantee their position among the more preferred methods medical specialists use in the detection and treatment of diabetes. It is not the author's intention to suggest they be replaced. However, it is a contention made by this thesis that a computerized, extremely capable system of imaging the retina can be developed to assist the diagnostician in making confident decisions, based on the most accurate information technologically possible.

An automated scanning system, such as that proposed, will propel the process of retinal imaging into the computer age, bringing with it all the implicit benefits that come with the use of these powerful, computational devices, not the least of which is their ability to provide a breathtaking display. With the technological advances made in both the laser and computer fields, their combined utility can be brought to bear on the problem of retinal imaging in the near term. By allowing specialists the ability to peer into the eye with an accuracy and acuity unlike any previously afforded, not only will the limitations of the current methods be resolved, but existing theories of the eye's connection to various other diseases, beyond diabetes, can then be researched.

Looking ahead, it may realistically be the theories surrounding diabetic retinopathy, the future considerations, that may most benefit from a device such as that proposed. Given that the features described herein are developed to their

potential, there may be untold limits to the utility of this imaging system as designed for medical specialists. With accurate mapping, sub-choroidal imaging, spectroscopy, and the ability to return a fully functional, color display of the retina, the progressive minds within the diabetes research and treatment field will be provided with a system to take them confidently into the future.

In retrospect, the specifications suggested herein are at the heart of what has been concluded by this study. They provide the entry issues to be addressed in the further development of this concept. It will be only through skilled, determined effort that this work make it past the simple 'concept stage' that it now finds itself in. What has been researched to this point is the direction, as best determined by the author, in which continued study might take. While all the information contained on these pages is considered accurate and current, it is to be kept in mind that new technological advances in any one of several fields included withinin the total system may provide an entirely new, scholarly direction for the study. May those that follow choose their steps wisely.

APPENDIX. DOCTOR SURVEY

DESIGN SPECIFICATION FOR AN AUTOMATED EYE SCANNER TO BE USED IN IMAGING THE RETINA

Researcher: Frank Dombrowski

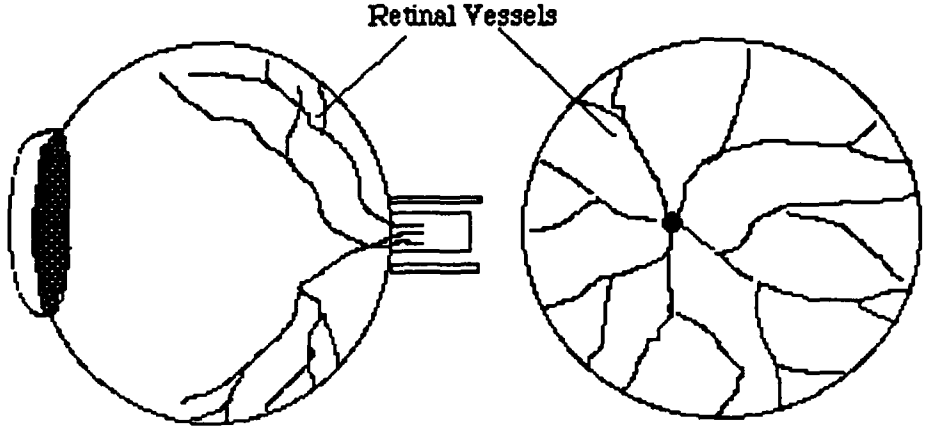
Comments on the Concept by:

Name:
Address:
Affiliated with
Phone #:

October 1988

BIOMETRICS

1. Please denote <u>desired scan coverage</u> for proper diagnosis



DUAL VIEW OF RETINA

2. Comments on the need for this size scanned area.

_____

_____

_____

_____

_____

3. Other issues that you feel may be a factor in the scan.

_____

_____

_____

_____

_____

GRAPHIC INTERFACE

1. What size screen would you consider minimal?

_____INCHES

2. Would you need a color display? **Yes** **No**

3. What graphic utilities would you like to see with the system?

Please comment on each as to your respective desires...

a) Enlargement

b) Template Overlays

c) Automated Template Comparison

d) Size of Characteristics to be detected

*e) Other*_____

*f) Other*_____

4. Would you like a lot of controls readily available or few controls with most standard features transparent to normal use?

5. What do you feel is the benefit of a graphic interface such as this?

SYSTEM SPECIFICATIONS

1. How many total patients do you estimate you could enroll in this system.....in one year? _____
.....in five years? _____

2. How many retinal images per patient?_____(1-year)
_____(5-year)

3. Would you use it with a personal computer? Y N
networked computer system? Y N
in your office? Y N
at a hospital? Y N

4. In your particlar realm of expertise, how do you most likely foresee the use of this system?

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